

## **REMARKS**

### **I. Support for the Amendments**

Claims 1-25 were originally in the application. Claims 1-20 were elected by the Applicants in the Response to the Election/Restriction Requirement, and the compound H-Ala<sub>10</sub>-Lys-OH was elected.

In the Office Action, mailed 25 February 2004, the Examiner withdrew claims 21-25 from consideration, as well as claims 2, 4-6, 8, 14, and 20, which were alleged not to read upon the elected compound. The Examiner examined claims 1, 3, 7, 9-13, and 15-19 on the merits.

Claims 2, 4-6, 8, 14, and 20-25 are non-elected claims withdrawn without prejudice to pursuing them in an appropriate divisional or continuation application. Claims 1, 11-13, and 15-18 have been amended, and new claims 26-73 have been added. No new matter has been added.

Claims 1, 3, 7, 9-13, 15-19, and 26-73 are presently in the application.

Support for amended claims 1, 11-13, and 15-18 can be found in the original specification and claims.

Support for new claims 26-74 can be found in the original specification and claims, particularly in the original language of claims 1, 3, 7, 9-13, and 15-19 as filed.

Additional support for amended claims 1 and 11-13 and new claims 27, 30, 34-41, 44, 48-55, 58, 59, 63-65, and 68-73 can be found, e.g., at page 17, lines 15-22; at page 21, lines 8-14; from page 23, line 16, to page 24, line 3; and in the Examples. Additional support for amended claims 1, and 16-18 and new claims 26, 27, 29-31, 39-42, 44, 45, 53-56, 58, 60, 61, and 70-73 can be found, e.g., at page 13, lines 11-23; at page 31, lines 6-24;

at page 34, lines 6-8 and lines 17-18; and elsewhere in the Examples. Additional support for amended claim 1 and new claims 27, 28, 30, 44, 58, 59, and 73 can be found, e.g., from page 8, line 17, to page 10, line 13; at page 11, lines 22-26; from page 12, line 12, to page 13, line 9; from page 15, lines 17, to page 17, line 1; and throughout the Examples. Additional support for new claims 32, 46, and 66 can be found, e.g., at page 14, lines 2-10; at page 26, lines 7-10; and in the Examples. Additional support for new claims 33, 47, and 67 can be found, e.g., from page 13, line 25, to page 14, line 2; on page 19, lines 8 and 26; and in the Examples. Additional support for new claims 34, 35, 48, 49, 68, and 69 can be found, e.g., at page 17, lines 15-22; from page 23, line 16, to page 24, line 3; and elsewhere in the Examples. Additional support for amended claims 11-13 and new claims 36-38, 50-52, and 63-65 can be found, e.g., at page 18, lines 17-21; from page 25, line 10, to page 26, line 5; and in the Examples. Additional support for amended claims 15-17 and new claims 39-41, 53-55, and 70-72 can be found, e.g., from page 14, line 12, to page 15, line 11; at page 18, lines 23-28; and in the Examples.

## **II. Status of the Claims**

Claims 1-25 were originally in the application. Claims 1-25 were subject to an election/restriction requirement, and Group I (claims 1-20) and the compound H-Ala<sub>10</sub>-Lys-OH were elected with traverse. In the Office Action, mailed 25 February 2004, the Examiner withdrew claims 21-25 from consideration, as well as claims 2, 4-6, 8, 14, and 20, which were alleged not to read upon the elected compound. The Examiner examined claims 1, 3, 7, 9-13, and 15-19 on the merits.

Claims 2, 4-6, 8, 14, and 20-25 are non-elected claims withdrawn without prejudice to pursuing them in an appropriate divisional or continuation application. Claims 1, 11-13, and 15-18 have been amended, and new claims 26-73 have been added. No new matter has been added.

Claims 1, 3, 7, 9-13, 15-19, and 26-73 are presently in the application.

### **III. The Information Disclosure Statements**

The Examiner has initialed the references cited on the Forms PTO-1449 filed with the Information Disclosure Statements on May 25, 2000, and on July 11, 2003. Applicants thank the Examiner for acknowledging these references.

### **IV. The Rejection of Claims 9 and 10 for Lack of Antecedent Basis Under 35 U.S.C. §112, Second Paragraph, Is Accommodated**

The Examiner has rejected claims 9 and 10 for lack of antecedent basis under 35 U.S.C. §112, second paragraph, because claims 1 and 11-13 recite the limitation “the support” and claims 9 and 10 recite “the solid support.” The Examiner suggested amendment of claim 1 to describe “the support” or “the solid support” for the solid phase synthesis.

Applicants have amended claims 1 and 11-13 to recite “the solid support.” Support for this amendment can be found in original claims 9 and 10 (and in original claim 1 by implication of the “solid phase” synthesis). Additional support can be found, e.g., at page 17, lines 15-22; at page 21, lines 8-14; from page 23, line 16, to page 24, line 3; and in the Examples.

Applicants respectfully submit that the present claims 9 and 10 fulfill the requirements of 35 U.S.C. §112, second paragraph, and request the Examiner’s reconsideration of these claims accordingly.

**V. The Rejection of Claims 1, 3, 7, 9-13, and 15-19 Under 35 U.S.C. §112, Second Paragraph, Is Traversed in Part and Accommodated in Part**

The Examiner has rejected claims 1, 3, 7, 9-13, and 15-19 under 35 U.S.C. §112, second paragraph, “as being indefinite for failing to point out and distinctly claim the subject matter which applicant regards as the invention.” Applicants have accommodated some of the remarks, but otherwise respectfully traverse this rejection.

**A. The Compound “H-Ala<sub>10</sub>-Lys-OH” and the Pre-Sequence**

First, it is alleged:

....At the outset, it is noted that the claims as drafted are unclear because the language is not drawn to the elected invention (a method of making the compound “H-Ala<sub>10</sub>-Lys-OH”). Thus, the claims should be amended so as to only be drawn to the elected invention (a method of making the compound “H-Ala<sub>10</sub>-Lys-OH”).

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In claim 1, it is unclear what is meant by “said C-terminal amino acid comprises a *presequence* comprising from 3 to 9 amino acid residues . . .”? Namely, the elected invention is a method of making the compound “H-Ala<sub>10</sub>-Lys-OH”. Additionally, it is unclear whether the 1st Ala or Lys is the C-terminal amino acid? In either case, the elected compound does not contain a “presequence” (i.e. from 3 to 9 amino acid residues?) attached to either Lys or Ala (whichever, Applicant regards as the C-terminal). Furthermore, it appears that the presequence in step (d) may be “optionally” cleaved from the formed peptide (elected “H-Ala<sub>10</sub>-Lys-OH”); which leaves open the option of the presequence being left on the elected peptide (“H-Ala<sub>10</sub>-Lys-OH”), which would then constitute an invention not drawn to the elected subject matter (a method of making the compound “H-Ala<sub>10</sub>-Lys-OH”). It is suggested that the term “presequence . . .” be deleted from step (b) of claim 1, as well as the language of step (d). [Pp. 2-3.]

Applicants have amended claim 1 to recite “H-Ala<sub>10</sub>-Lys-OH,” and claims 3, 7, 9-13, and 15-19 are dependent on claim 1. (New claims 26-29, 31, 42, 43 and 73 also read on “H-Ala<sub>10</sub>-Lys-OH.”)

However, for various reasons, Applicants respectfully continue to traverse the requirement for an election of species. Moreover, Applicants respectfully traverse the new restriction as it pertains to claims 2, 4-6, 8, 14, and 20, which were subsequently withdrawn by the Examiner in the Office Action mailed February 25, 2004.

First, Applicants wish to draw the Examiner's attention to the fact that the present invention does not focus solely and exclusively on the synthesis of a given peptide having a specific sequence, but rather encompasses a method for the synthesis of a potentially infinite number of peptides with diverse sequences. In essence, the invention is a process or method and not a product-by-process, where the specific compounds disclosed in the application are recognized in the art. A search would not be a search for a specific sequence, but rather a search for a method.

Applicants respectfully submit that the Patent Office has misinterpreted the distinction between a claim for a process of making a particular chemical compound and a claim for a process for making a class of chemical entities.

In the Election/Restriction Requirement, mailed July 15, 2003, it was stated:

Applicant is required to select a single compound to be examined, whether a process (Group I) or compound (Group II-VI) is elected, and to identify all claims readable on that compound (if Group I is elected). For instance, if group Group I (or any other Group) is elected, then all variables of the structure X-AA1-AA2.....AAn-Y," must be specifically identified, so that a search of the structure (peptide), and processes of making the peptide, may be conducted. This requirement is not to be taken as an election of species, but rather as an election of a single invention, since each compound is assumed to be patentably distinct invention, in the absence of evidence to the contrary.  
[Detailed Action, p. 4]

Applicants respectfully submit that it is irrelevant whether the myriad possible

products of the present invention are patentably distinct from one another. Rather, the invention is directed to a process. Here Applicants have provided quite a number of examples of using the claimed process (as described in the original specification and claims) to produce a variety of very different peptides. (For the record, Applicants also previously traversed the election between the Groups.) It is alleged that “each compound is assumed to be patentably distinct invention,” but the proper focus should be not on “each compound” but on the process, and whether the process is patentably distinct over the process itself, which cannot be the case. Certainly, the search of a process, such as the single process described in original claim 1, which was the only independent claim of Group I, would not pose a serious burden on the Examiner. Moreover, many compounds exemplified in the specification are recognized in the art.

One could analogise the present situation to a claim for a method of performing a polymerase chain reaction (PCR). While different PCR products might be patentably distinct from each other, one would not restrict the claim to the PCR process to one particular product. MPEP §803.04 and similar provisions are irrelevant. The process is the subject matter – not each sequence within the multitude of different reactions and their resulting products.

The present requirement renders meaningful patent protection impossible and would force the Applicants to file and prosecute a potentially infinite number of applications, each with a separate set of claims to the production of a single, specific compound. Such a requirement is both extremely expensive for the Applicants and an inefficient use of Patent & Trademark Office resources. Even assuming that the Applicants could afford the time and money to file an application to cover the production of each and every possible compound, such a procedure would present a serious, if not impossible, burden on the Patent & Trademark Office to provide the necessary staffing and resources to process the myriad applications.

More specifically, the present invention is concerned with solid phase peptide synthesis (SPPS). A general problem in solid phase peptide synthesis (SPPS) has been the occurrence of “difficult” peptide sequences. The synthesis of such “difficult” peptide sequences has been associated with incomplete coupling and de-protection reactions. (For a discussion of “difficult” sequences, see the specification from page 6, line 25, to page 7, line 23; at page 8, lines 6-13; and in the Examples from page 44, line 4, to page 48, line 3.) Together, these problems lead to highly complicated product mixtures containing several deletion sequences (peptides missing one or more amino acids) in addition to the target peptide. In such product mixtures, the deletion sequences are very closely associated with the target peptide sequence and thus virtually impossible to eliminate in the subsequent purification process.

The incomplete coupling and de-protection reactions are due to aggregation of the growing peptide chains during the solid phase synthesis. The tendency to aggregate is very high for “difficult” peptide sequences and the aggregation phenomenon is based on beta-sheet formation. This aggregation of the growing peptide chains causes the coupling and de-protection reaction rates to decrease dramatically, thus rendering them “difficult.” In many instances, this aggregation results in the peptide chain’s becoming periodically inaccessible for further synthesis.

Many attempts have been made to improve the procedures involved in SPPS and prior art has described optimizations of, for example, 1) reaction conditions or the 2) solid support to which the growing peptide is anchored. However, nothing in the prior art describes a method wherein the step of **selecting a pre-sequence** provides for an improved peptide synthesis.

This feature of actively and purposefully **selecting a pre-sequence** is a key feature

of the present invention, and it is one feature that distinguishes the process of the present claim 1 from the prior art. Indeed, it is this particular novel feature that provides the superior peptide synthesis process of the present invention having reduced coupling times, i.e., very fast coupling rates. Subsequently cleaving the pre-sequence from the remaining peptide is only one possible embodiment represented by the present invention.

Claim 1 has been amended to define the pre-sequence for the elected compound as the Lys residue itself, in order to accommodate the Examiner's remarks. Claims 3, 7, 9-13, and 15-19 are dependent on claim 1, as is new claim 26, and new claims 27-29 and 73 also address this issue in a different way.

Nonetheless, for the reasons outlined *supra*, the Applicants likewise traverse the remarks concerning the pre-sequence.

Applicants also respectfully request reconsideration of claims 2, 4-6, 8, 14, and 20, which were subsequently withdrawn by the Examiner.

Applicants respectfully submit that the present claims 1, 3, 7, 9-13, and 15-19 fulfill the requirements of 35 U.S.C. § 112, second paragraph, and request the Examiner's reconsideration of these claims accordingly.

B. The N-alpha-Protected C-Terminal Amino Acid

It is alleged:

In claim 1, it is unclear what is meant by "the C-terminal amino acid in the *form* of an N-alpha-protected reactive derivative"? Additionally, it is unclear whether the 1st Ala or Lys is the C-terminal amino acid? Namely, it is unclear if the C-terminal amino acid has an "N-alpha-protected reactive



derivative” or is just similar to such chemical modification? In either case, the claim must be amended to clarify the structure of the C-terminal amino acid. [P. 3; emphasis in original.]

Applicants have amended claim 1 to accommodate the Examiner’s remarks and have removed the language “reactive derivative” in favor of “N-alpha-protected C-terminal amino acid.” Claims 3, 7, 9-13, and 15-19 are dependent on claim 1.

In addition, Applicants respectfully submit that, in accordance with accepted sequence conventions and standard definitions and practices in the art, the peptide sequences in the specification and claims are presented with the amino acid residues shown from the N-terminal residue on the left to the C-terminal residue on the right. Thus, for the sequence “H-Ala<sub>10</sub>-Lys-OH,” the C-terminal amino acid is Lys, while the first Ala (Ala<sub>1</sub>) is the N-terminal amino acid. The “N-alpha-protected C-terminal amino acid” would be an N-alpha-protected Lys. This practice conforms to the internationally accepted conventions within the art.

Applicants respectfully submit that the present claims 1, 3, 7, 9-13, and 15-19 fulfill the requirements of 35 U.S.C. §112, second paragraph, and request the Examiner’s reconsideration of these claims accordingly.

#### C. The Coupling by Means of a Linker

It is alleged:

In claim 1, it is unclear what is meant by “coupling . . . optionally by means of a *linker*”? The claims must be amended to clarify whether the invention is coupled by a linker or not. [P. 3; emphasis in original.]

Applicants have amended claim 1 to accommodate the Examiner's remarks and have removed the language "optionally by means of a linker." Claims 3, 7, 9-13, and 15-19 are dependent on claim 1.

Applicants respectfully submit that the present claims 1, 3, 7, 9-13, and 15-19 fulfill the requirements of 35 U.S.C. §112, second paragraph, and request the Examiner's reconsideration of these claims accordingly.

## **VI. The Examiner's Remarks Regarding Allowable Subject Matter**

The Examiner states:

It is noted that claims 1, 3, 7, 9-13, and 15-19 have only been examined as drawn to the elected invention (a method of making the compound "H-Ala<sub>10</sub>-Lys-OH"). The present method of making the compound "H-Ala<sub>10</sub>-Lys-OH" was found to be free of the prior art, based on the steps of the method as claimed (notwithstanding the rejections above as to certain steps not being drawn to the elected invention). As allowable subject matter has been indicated, applicant's reply must either comply with all formal requirements or specifically traverse each requirement not complied with. See 37 CFR 1.111(b) and MPEP § 707.07(a). [P. 4.]

Applicants thank the Examiner for the above remarks. Applicants have amended claims 1, 11-13, and 15-18 and respectfully submit that the amendments place the present claims 1, 3, 7, 9-13, and 15-19 in a condition for allowance. Accordingly, Applicants respectfully request the Examiner's reconsideration of these claims.

# CONCLUSION

It is believed that all outstanding rejections have been addressed by this submission and that all the claims are in condition for allowance. If discussion of any amendment or remark made herein would advance this important case to allowance, the Examiner is invited to call the undersigned as soon as convenient.

In view of the foregoing amendments and remarks, the present application is respectfully considered in condition for allowance. An early reconsideration and notice of allowance are earnestly solicited.

Applicants hereby request a three-month extension of time for the Amendment and submit the requisite fee herewith. If, however, a petition for an additional extension of time is required, then the Examiner is requested to treat this as a conditional petition for an additional extension of time. Although it is not believed that any fee is required, in addition to the fee submitted herewith, to consider this submission, the Commissioner is hereby authorized to charge our deposit account no. 04-1105 should any fee be deemed necessary.

Respectfully submitted,



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